

FILE 'USPAT' ENTERED AT 21:12:30 ON 12 SEP 1997

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\* WELCOME TO THE \*  
\* U. S. PATENT TEXT FILE \*  
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=> s ((tumor? or tumour?)(w)necro? factor?)(5a)receptor?

19357 TUMOR?

1789 TUMOUR?

8023 NECRO?

390714 FACTOR?

1684 NECRO? FACTOR?

(NECRO?(W)FACTOR?)

28325 RECEPTOR?

L1 73 ((TUMOR? OR TUMOUR?)(W)NECRO?

FACTOR?)(5A)RECEPTOR?

=> s l1 and (dna? or cdna? or rna? or mrna? or clon?)

20738 DNA?

6513 CDNA?

11909 RNA?

5858 MRNA?

17106 CLON?

L2 70 L1 AND (DNA? OR CDNA? OR RNA? OR MRNA?  
OR CLON?)

=> d 1-20

1. 5,665,859, Sep. 9, 1997, Molecules influencing the shedding of the TNF receptor, their preparation and their use; David Wallach, et al., 530/328; 435/69.2, 226; 530/327, 350 :IMAGE AVAILABLE:

2. 5,663,070, Sep. 2, 1997, Recombinant production of a soluble splice variant of the Fas (Apo-1) antigen, fas TM; Philip J. Barr, et al., 435/325, 69.1, 253.3, 254.11, 320.1, 348, 358, 361; 536/23.5 :IMAGE AVAILABLE:

3. 5,661,004, Aug. 26, 1997, Lymphotoxin-.beta., lymphotoxin-.beta. complexes, pharmaceutical preparations and therapeutic uses thereof; Jeffrey Browning, et al., 435/69.1; 536/23.5 :IMAGE AVAILABLE:

4. 5,658,949, Aug. 19, 1997, Inhibition of tumor necrosis factor by retinoic acid; Bharat B. Aggarwal, 514/557, 825, 895, 903 :IMAGE AVAILABLE:

5. 5,654,407, Aug. 5, 1997, Human anti-TNF antibodies; Petra Boyle, et al., 530/388.15; 424/142.1, 145.1, 158.1; 435/335; 530/388.23, 388.24 :IMAGE AVAILABLE:

6. 5,652,353, Jul. 29, 1997, \*\*DNAs\*\* encoding tumor necrosis factor-.alpha. muteins; Walter Fiers, et al., 536/23.5; 435/69.5, 172.3, 252.3, 320.1; 935/11, 22, 70, 73 :IMAGE AVAILABLE:

7. 5,652,225, Jul. 29, 1997, Methods and products for nucleic acid delivery; Jeffrey M. Isner, 514/44; 424/93.2; 435/172.1, 172.3, 320.1; 536/23.5, 23.51; 604/51, 52, 53; 935/9, 22, 32, 33, 34, 52, 57 :IMAGE AVAILABLE:

8. 5,652,210, Jul. 29, 1997, Soluble splice variant of the Fas (APO-1)

antigen, Fas.DELTA.TM; Philip J. Barr, et al., 514/2; 435/69.1; 514/8; 530/350, 395 :IMAGE AVAILABLE:

9. 5,650,316, Jul. 22, 1997, Uses of triplex forming oligonucleotides for the treatment of human diseases; Bharat B. Aggarwal, et al., 435/375, 6, 7.23; 514/44; 536/24.31, 24.32, 24.33, 24.5 :IMAGE AVAILABLE:

10. 5,643,875, Jul. 1, 1997, Human therapeutic uses of bactericidal/permeability increasing (BPI) protein products; Nadav Friedmann, et al., 514/12; 424/85.1, 85.2, 529, 534; 514/21, 921; 530/324, 325, 351, 820 :IMAGE AVAILABLE:

11. 5,641,751, Jun. 24, 1997, Tumor necrosis factor inhibitors; George A. Heavner, 514/13, 12, 14, 15, 16, 17, 18; 530/324, 325, 326, 327, 328, 329, 330 :IMAGE AVAILABLE:

12. 5,632,994, May 27, 1997, Fas associated proteins; John C. Reed, et al., 424/198.1, 185.1, 192.1; 435/7.1, 7.2, 7.9; 530/387.3, 387.9 :IMAGE AVAILABLE:

13. 5,626,843, May 6, 1997, Treatment of autoimmune diseases, including AIDS, by removal of interferons, TNFs and receptors therefor; Simon V. Skurkovich, et al., 424/140.1; 604/6 :IMAGE AVAILABLE:

14. 5,620,889, Apr. 15, 1997, Human anti-Fas IgG1 monoclonal antibodies; David H. Lynch, et al., 435/332; 424/144.1; 435/334, 343.2; 530/387.1, 388.2, 388.23, 388.24, 388.75 :IMAGE AVAILABLE:

15. 5,618,715, Apr. 8, 1997, Oncostatin M and novel compositions having anti-neoplastic activity; Mohammed Shoyab, et al., 435/325, 69.1, 69.4, 320.1, 348, 360, 364, 365.1; 530/300, 351; 536/23.1, 23.51 :IMAGE AVAILABLE:

16. 5,616,491, Apr. 1, 1997, Knockout mice; Tak W. Mak, et al., 435/354, 172.3, 320.1, 355; 536/23.1; 800/2, DIG.1; 935/22, 70 :IMAGE AVAILABLE:

17. 5,610,281, Mar. 11, 1997, Antibodies for modulating heterotypic E-cadherin interactions with human T lymphocytes; Michael B. Brenner, et al., 530/388.85; 424/141.1, 145.1, 154.1, 156.1; 530/387.1, 388.1, 388.22, 388.23, 388.75 :IMAGE AVAILABLE:

18. 5,609,847, Mar. 11, 1997, Treatment methods using metal-binding targeted polypeptide constructs; Benjamin A. Belinka, Jr., et al., 424/1.69, 1.11, 9.1; 530/300, 311; 534/10 :IMAGE AVAILABLE:

19. 5,606,023, Feb. 25, 1997, Mutant tumor necrosis factor proteins; Mann-Jy Chen, et al., 530/351; 424/85.2; 435/69.52 :IMAGE AVAILABLE:

20. 5,605,690, Feb. 25, 1997, Methods of lowering active TNF-.alpha.

levels in mammals using \*\*tumor\*\* \*\*necrosis\*\* \*\*factor\*\*  
\*\*receptor\*\*;  
Cindy A. Jacobs, et al., 424/134.1; 435/69.7; 514/12, 825; 530/350,  
387.3, 866, 868 :IMAGE AVAILABLE:

=> d 20 ab

US PAT NO: 5,605,690 :IMAGE AVAILABLE: L2: 20  
of 70

#### ABSTRACT:

A method for treating TNF-dependent inflammatory diseases in a  
mammal by  
administering a TNF antagonist, such as soluble TNFR.

=> d 20 clms

US PAT NO: 5,605,690 :IMAGE AVAILABLE: L2: 20  
of 70

#### CLAIMS:

##### CLMS(1)

We claim:

1. A method for lowering the levels of active TNF-.alpha. in a  
mammal in  
need thereof which comprises administering to said mammal a TNF-  
lowering  
amount of a TNF antagonist selected from the group consisting of:  
(a) a TNF receptor comprising the sequence of amino acids 3-163 of  
SEQ  
ID NO:1; and  
(b) a chimeric antibody comprising a TNF receptor according to (a)  
fused  
to the constant domain of an immunoglobulin molecule.

##### CLMS(2)

2. A method for lowering the levels of active TNF-.alpha. in a  
mammal in  
need thereof which comprises administering to said mammal a TNF-  
lowering  
amount of a TNF receptor comprising the sequence of amino acids 3-  
163 of  
SEQ ID NO:1.

##### CLMS(3)

3. A method for lowering the levels of active TNF-.alpha. in a  
mammal in  
need thereof which comprises administering to said mammal a TNF-  
lowering  
amount of a chimeric antibody comprising a TNF receptor  
comprising the  
sequence of amino acids 3-163 of SEQ ID NO:1 fused to the  
constant domain  
of an immunoglobulin molecule.

##### CLMS(4)

4. A method for lowering the levels of active TNF-.alpha. in a  
mammal  
having arthritis, which comprises administering to such mammal a  
therapeutically effective amount of a TNF-antagonist selected from  
the  
group consisting of:  
(a) a TNF receptor comprising the sequence of amino acids 3-163 of  
SEQ  
ID NO:1; and

(b) a chimeric antibody comprising a TNF receptor according to (a)  
fused  
to the constant domain of an immunoglobulin molecule.

##### CLMS(5)

5. A method for lowering the levels of active TNF-.alpha. in a  
mammal  
having arthritis, which comprises administering to said mammal a  
TNF-lowering amount of a TNF receptor comprising the sequence of  
amino  
acids 3-163 of SEQ ID NO:1.

##### CLMS(6)

6. A method for lowering the levels of active TNF-.alpha. in a  
mammal  
having arthritis, which comprises administering to said mammal a  
TNF-lowering amount of a chimeric antibody comprising a TNF  
receptor  
comprising the sequence of amino acids 3-163 of SEQ ID NO:1  
fused to the  
constant domain of an immunoglobulin molecule.

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US PAT NO: 5,605,690 :IMAGE AVAILABLE: L2: 20  
of 70

DATE ISSUED: Feb. 25, 1997

TITLE: Methods of lowering active TNF-.alpha. levels in  
mammals

using \*\*tumor\*\* \*\*necrosis\*\* \*\*factor\*\* \*\*receptor\*\*

INVENTOR: Cindy A. Jacobs, Seattle, WA  
Craig A. Smith, Seattle, WA

ASSIGNEE: Immunex Corporation, Seattle, WA (U.S. corp.)

APPL-NO: 08/385,229

DATE FILED: Feb. 8, 1995

REL-US-DATA: Continuation of Ser. No. 946,236, Sep. 15, 1992,  
abandoned, which is a continuation-in-part of Ser. No.  
523,635, May 10, 1990, Pat. No. 5,395,760, which is a  
continuation-in-part of Ser. No. 421,417, Oct. 13, 1989,  
abandoned, which is a continuation-in-part of Ser. No.  
405,370, Sep. 11, 1989, abandoned, which is a  
continuation-in-part of Ser. No. 403,241, Sep. 5, 1989,  
abandoned.

INT-CL: :6: A61K 39/395; A61K 38/00; C12P 21/04; C07K  
14/715

US-CL-ISSUED: 424/134.1; 435/69.7; 514/12, 825; 530/350,  
387.3, 866, 868

US-CL-CURRENT: 424/134.1; 435/69.7; 514/12, 825; 530/350,  
387.3, 866, 868

SEARCH-FLD: 435/69.1, 69.7, 172.3, 240.27; 424/85.1, 134.1;  
530/351,

387.3, 868; 935/9, 12, 15

#### REF-CITED:

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5,512,544	4/1996	Wallach et al.	

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WO9013575	11/1990	World Intellectual Property Organization	C07K 15/14

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- Smith et al., "Blocking of HIV-1 Infectivity by a Soluble, Secreted Form of the CD4 Antigen", Science 238:1704-1707.
- ART-UNIT: 186
- PRIM-EXMR: Lila Feisee
- ASST-EXMR: John Lucas
- LEGAL-REP: Stephen L. Malaska

## ABSTRACT:

A method for treating TNF-dependent inflammatory diseases in a mammal by

administering a TNF antagonist, such as soluble TNFR.  
6 Claims, 7 Drawing Figures

=> d 21-30

21. 5,597,899, Jan. 28, 1997, Tumor necrosis factor muteins; David Banner, et al., 530/351; 435/69.1, 69.5; 530/402 :IMAGE AVAILABLE:

22. 5,593,656, Jan. 14, 1997, Metal-binding targeted polypeptide constructs; Benjamin A. Belinka, Jr., et al., 424/1.69, 9.1, 9.3, 9.4; 530/300, 324, 325, 326, 327, 328, 329, 330; 534/10, 14, 15 :IMAGE AVAILABLE:

23. 5,582,998, Dec. 10, 1996, Monoclonal antibodies against human TNF-binding protein I (TNF-BP I) and immunoassays therefor; G unther Adolf; 435/7.1, 7.92, 7.94, 70.21, 334; 436/811, 815; 530/388.1 :IMAGE AVAILABLE:

24. 5,580,722, Dec. 3, 1996, Methods of determining chemicals that modulate transcriptionally expression of genes associated with cardiovascular disease; J. Gordon Foulkes, et al., 435/6, 91.1, 91.2; 935/77, 78 :IMAGE AVAILABLE:

25. 5,578,461, Nov. 26, 1996, Gene manipulation and expression using genomic elements; Stephen Sherwin, et al., 435/69.1, 172.3, 244, 320.1; 536/23.1, 24.1; 935/28, 33, 55 :IMAGE AVAILABLE:

26. 5,578,288, Nov. 26, 1996, Metal-binding targeted polypeptide constructs; Benjamin A. Belinka, Jr., et al., 424/1.69, 1.11; 530/300, 326, 327, 328; 534/10, 14 :IMAGE AVAILABLE:

27. 5,565,334, Oct. 15, 1996, Enhancer sequence for modulating expression in epithelial cells; Donald Kufe, et al., 435/69.1, 320.1, 371; 536/23.1, 23.2, 24.1, 24.5 :IMAGE AVAILABLE:

28. 5,563,039, Oct. 8, 1996, TNF receptor-associated intracellular signaling proteins and methods of use; David V. Goeddel, et al., 435/7.1, 6, 69.1, 252.3, 320.1; 436/501; 530/300, 350 :IMAGE AVAILABLE:

29. 5,557,032, Sep. 17, 1996, Knockout mice; Tak W. Mak, 800/2; 424/9.2; 435/172.3, 320.1; 800/DIG.1, DIG.4; 935/11, 70 :IMAGE AVAILABLE:

30. 5,543,139, Aug. 6, 1996, 5.5 kD TNF degradation product; John P. Fruehauf, 424/85.1, 520; 530/300, 350, 351, 402, 407 :IMAGE AVAILABLE:

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31. 5,541,085, Jul. 30, 1996, Method for preparing orphan receptor ligands; Richard D. Holly, et al., 435/69.1, 6, 69.5, 172.3 :IMAGE AVAILABLE:

32. 5,538,863, Jul. 23, 1996, Expression system comprising mutant yeast strain and expression vector encoding synthetic signal peptide; Virginia L. Price, 435/69.1, 254.2, 254.21, 320.1; 536/23.1, 23.4, 23.7, 24.1 :IMAGE AVAILABLE:

33. 5,536,657, Jul. 16, 1996, Recombinant \*\*DNA\*\* encoding human receptor for interleukin-12; Anne O. Chua, et al., 435/252.3, 69.1, 69.52, 320.1; 536/23.5 :IMAGE AVAILABLE:

34. 5,521,295, May 28, 1996, Nucleic acids encoding hybrid receptor molecules; Robert E. Pacifici, et al., 536/23.4; 435/7.1, 172.3, 320.1; 530/350 :IMAGE AVAILABLE:

35. 5,519,000, May 21, 1996, Tumor necrosis factor inhibitors; George A. Heavner, et al., 514/12, 13, 14, 15, 16, 17, 18; 530/324, 326, 328, 329, 330 :IMAGE AVAILABLE:

36. 5,506,340, Apr. 9, 1996, Tumor necrosis factor inhibitors; George A. Heavner, 530/324, 325, 326, 327, 328, 329, 330 :IMAGE AVAILABLE:

37. 5,486,595, Jan. 23, 1996, Tumor necrosis factor inhibitors; George A. Heavner, 530/324, 325, 326, 327, 328, 329, 330 :IMAGE AVAILABLE:

38. 5,486,463, Jan. 23, 1996, TNF-muteins; Werner Lesslauer, et al., 435/69.5, 252.33, 320.1; 530/351; 536/23.5, 23.51 :IMAGE AVAILABLE:

39. 5,478,925, Dec. 26, 1995, Multimers of the soluble forms of TNF receptors, their preparation and pharmaceutical compositions containing them; David Wallach, et al., 530/351; 424/85.1, 158.1, 450 :IMAGE AVAILABLE:

40. 5,470,829, Nov. 28, 1995, Pharmaceutical preparation; Per Prisell, et al., 514/12; 424/85.1; 514/2, 8, 21; 525/54.1 :IMAGE AVAILABLE:

41. 5,470,730, Nov. 28, 1995, Method for producing T.sub.H - independent cytotoxic T lymphocytes; Phillip D. Greenberg, et al., 435/172.3; 424/93.21; 435/69.1, 69.52, 70.4, 252.3, 320.1 :IMAGE AVAILABLE:

42. 5,460,965, Oct. 24, 1995, \*\*DNA\*\* and \*\*RNA\*\* encoding proteins useful in the regulation of KB-containing genes, and cells containing same; Gary J. Nabel, et al., 435/372.3, 172.3, 252.3, 252.33; 536/23.5 :IMAGE AVAILABLE:

43. 5,457,035, Oct. 10, 1995, Cytokine which is a ligand for OX40; Peter R. Baum, et al., 435/69.5, 252.3, 320.1, 364; 530/351; 536/23.5; 935/9 :IMAGE AVAILABLE:

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45. 5,451,506, Sep. 19, 1995, Oncostatin M and novel compositions having anti-neoplastic activity; Mohammed Shoyab, et al., 43/57.23, 7.1, 7.21, 960; 530/351 :IMAGE AVAILABLE:

46. 5,449,761, Sep. 12, 1995, Metal-binding targeted polypeptide constructs; Benjamin A. Belinka, Jr., et al., 534/10; 530/300, 326, 327, 328, 399, 408; 534/14, 15; 564/18, 23, 26, 27, 28 :IMAGE AVAILABLE:

47. 5,447,851, Sep. 5, 1995, \*\*DNA\*\* encoding a chimeric polypeptide comprising the extracellular domain of TNF receptor fused to IgG, vectors, and host cells; Bruce A. Beutler, et al., 435/69.7, 69.5, 320.1, 328, 365; 530/300, 351; 536/23.4 :IMAGE AVAILABLE:

48. 5,428,012, Jun. 27, 1995, Oncostatin M and novel compositions having anti-neoplastic activity; Mohammed Shoyab, et al., 514/12; 424/85.1, 85.5; 514/21; 530/350 :IMAGE AVAILABLE:

49. 5,422,104, Jun. 6, 1995, TNF-mutins; Walter Fiers, et al., 424/85.1; 435/69.5; 530/351 :IMAGE AVAILABLE:

50. 5,395,760, Mar. 7, 1995, \*\*DNA\*\* encoding \*\*tumor\*\*  
\*\*necrosis\*\*  
\*\*factor\*\*-.alpha. and -.beta. \*\*receptors\*\*; Craig A. Smith, et al., 435/365; 424/85.1; 435/69.4, 172.3; 530/351, 388.23; 536/23.51 :IMAGE AVAILABLE:

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51. 5,380,747, Jan. 10, 1995, Treatment for atherosclerosis and other cardiovascular and inflammatory diseases; Russell M. Medford, et al., 514/423, 210, 212, 315, 476, 477 :IMAGE AVAILABLE:

52. 5,378,603, Jan. 3, 1995, Method and composition for identifying substances which activate transcription of the LDL receptor gene; Michael S. Brown, et al., 435/6, 4, 29, 172.3; 436/817; 935/76, 79, 82 :IMAGE AVAILABLE:

53. 5,374,423, Dec. 20, 1994, Method of using cytokine receptors on microorganism; Gary R. Klimpel, et al., 424/85.1, 193.1, 197.11, 234.1, 257.1, 258.1, 274.1; 435/252.1, 252.8, 255.4, 849, 879, 922 :IMAGE AVAILABLE:

54. 5,359,039, Oct. 25, 1994, Isolated poxvirus A53R-equivalent tumor necrosis factor antagonists; Craig A. Smith, et al., 530/350; 424/186.1, 232.1; 530/826; 536/23.72; 930/220 :IMAGE AVAILABLE:

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\*\*receptor\*\*  
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21 :IMAGE AVAILABLE:

56. 5,324,818, Jun. 28, 1994, Proteins useful in the regulation of .kappa.B-containing genes; Gary J. Nabel, et al., 530/350; 435/172.3; 935/11, 34, 36 :IMAGE AVAILABLE:

57. 5,270,038, Dec. 14, 1993, **Tumor** **necrosis** **factor**  
**receptors** on microorganisms; Gary R. Klimpel, et al., 424/85.1, 234.1, 257.1, 258.1, 274.1; 435/252.1, 252.8, 255.4, 849, 879, 922 :IMAGE AVAILABLE:

58. 5,256,545, Oct. 26, 1993, Sterol Regulatory Elements; Michael S. Brown, et al., 435/69.1, 172.3, 252.3, 320.1, 358; 536/24.1; 935/36, 43 :IMAGE AVAILABLE:

59. 5,248,671, Sep. 28, 1993, Methods and compositions for treatment of cancer using oligonucleotides; Larry J. Smith, 514/44 :IMAGE AVAILABLE:

60. 5,246,701, Sep. 21, 1993, Method for inhibiting production of IgE by using IL-9 inhibitors; Bernard Dugas, et al., 424/158.1, 85.2, 173.1, 805; 514/8, 21; 530/388.22, 388.23 :IMAGE AVAILABLE:

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62. 5,135,917, Aug. 4, 1992, Interleukin receptor expression inhibiting antisense oligonucleotides; Ronald M. Burch, 514/44; 530/351; 536/23.5, 24.5 :IMAGE AVAILABLE:

63. 5,135,915, Aug. 4, 1992, Method for the treatment of grafts prior to transplantation using TGF-.beta.; Christine W. Czarniecki, et al., 514/21; 424/85.1; 435/371, 372; 514/12; 530/399; 604/19, 48 :IMAGE AVAILABLE:

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